WHAT IS CLAIMED IS:

1.   A system for dispensing nanoliter-sized droplets on a surface in a precise pattern of non-overlapping spots to form a two

5   dimensional miniarray assay, comprising:

a spotter device comprising a print head for making said miniarray assays, said print head comprises pipette-based dispensers;

a robotic or mechanical arm carrying said print head; and

a working platform comprising regions or substations to

10   perform functions selected from the group consisting of holding miniarray substrates, loading samples, loading tips, cleaning tips and discarding tips.

15   2.   The system of claim 1, wherein said pipette-based dispensers are arranged in at least one row.

3.   The system of claim 1, wherein said pipette-based

20   dispensers can operate simultaneously to load microliter quantities of

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sample analyte reagents in solution and to dispense nanoliter quantities of said reagent solutions on the surface of the miniarray substrate.

5   4.   The system of claim 1, wherein said pipette-based dispensers have tips selected from the group consisting of disposable tips that can be ejected and replaced automatically and fixed tips that are cleaned and dried between sample loadings.

10   5.   The system of claim 1, wherein said robotic or mechanical arm moves laterally and vertically in relation to said working platform.

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6.   The system of claim 1, wherein said print head is activated by a method selected from the group consisting of actuation by remote syringe pumps that provide vacuum or pressure to said pipette-based dispensers, mechanically activated by minute pistons that are 20   fixed to said pipette-based dispensers, and hydraulically actuated by

remote syringe pumps connected to the pipetter pistons of said pipette-based dispensers.

5   7.   A method for forming a miniarray wherein each known location or spot in said miniarray contains an analyte specific reagent for detecting an analyte in a sample, comprising the steps of:

(a) aspirating a solution of each analyte specific reagent with a pipette-based dispensers;

10   (b) pressuring a small defined droplet of said analyte specific reagent from the narrow opening of the tip of said pipette-based dispensers;

(c) touching said droplet to the surface of the miniarray substrate with an action effective to release said droplet, thereby 15 spotting a specific location in said miniarray with a specific volume of said analyte specific reagent; and

(d) repeating steps (a) to (c) until said miniarray is fabricated.

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8. The method of claim 7, further comprising after step (c) a step of replacing or cleaning the tips of said pipette-based dispensers.

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9. The method of claim 7, wherein said pipette-based dispensers are arranged in one, or more than one, row.

10. The method of claim 7, wherein said pipette-based dispensers can operate simultaneously to load microliter quantities of sample reagents in solution and to dispense nanoliter quantities of said reagent solutions on the surface of the miniarray substrate.

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11. The method of claim 7, wherein said pipette-based dispensers have tips selected from the group consisting of disposable tips that can be ejected and replaced automatically and fixed tips that are cleaned and dried between sample loadings.

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12. The method of claim 7, wherein releasing of said droplet is performed by ejecting sufficient volume from the tip of said pipette-based dispensers to cause said droplet to release by gravity.

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13. The method of claim 7, wherein releasing of said droplet is performed by applying electromechanical force to the tip of said pipette-based dispensers to cause said droplet to release by gravity, wherein said electromechanical force is selected from the group consisting of vibration, piezoelectric pressure, and rapid mechanical actuation.

14. The method of claim 7, wherein said pipette-based dispensers are carried by a robotically controlled apparatus that provides lateral and vertical motions, thereby automating the loading of multiple reagent samples, the replacement or cleaning of pipette tips, and the spotting of multiple miniarrays under programmed instructions.

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15. The method of claim 7, wherein said miniarray achieves a smaller, more condensed distribution by interspersing successive dispensing of reagents onto the array in regions between the spots dispensed previously.

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16. The method of claim 7, wherein tips of said pipette-based dispensers are spaced 9 mm or 4.5 mm center to center to load multiple reagent samples from standard 96 well or 384 well plates.

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17. The method of claim 7, wherein said pipette-based dispensers are stationary, except for vertical motion, and miniarray substrates and reagent samples are moved under said dispensers by a robotic apparatus that moves under programmed instructions.

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18. The method of claim 7, wherein said miniarray substrate is selected from the group consisting of coated microscope slides, flexible membranes, rigid glass, plastics, semi-rigid film, paper-

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based printing substrates, semi-rigid printing materials, photographic paper and high quality computer printing papers.

5   19. The method of claim 7, wherein said analyte specific reagent comprises material selected from the group consisting of antibodies that bind to selected proteins of the analyte sample and polynucleotides complementary to sequences of the analyte sample, wherein said antibodies or polynucleotides are used to detect and

10   measure the relative frequency with which specific genes are expressed in the sample.

          20. The method of claim 7, wherein said analyte sample

15   comprises material selected from the group consisting of total RNA, mRNA, cDNA probes made from RNA transcripts, intracellular proteins and secreted proteins.

20   21. The method of claim 20, wherein two or more analyte samples are labeled differently and compared by competitive binding to

the same miniarray to determine relative gene expression levels between said samples.

5   22. The method of claim 21, wherein said samples are labeled by a means selected from the group consisting of isotopes, indirect labeling haptens, direct fluorescent reagents, indirect fluorescent reagents, quantum dots and nanogold.

10   23. A method of diagnosis for specific tissue or condition using specialized diagnostic miniarrays targeted to the analysis of said tissue or condition, comprising the steps of:

          (a) preparing one or more set of gene specific elements that

15   correspond to genes known to be significantly up-regulated or down-regulated in said tissue or condition relative to control sample;

          (b) preparing one or more sets of gene specific elements that correspond to genes commonly expressed in both control sample and in said tissue or said condition;

20   (c) arranging the gene specific elements of (a) and (b) on a miniarray; and

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(d) applying a target sample to said miniarray, wherein detection of a visually distinct image from said miniarray indicates the presence of said tissue or condition.

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24. The method of claim 23, wherein said condition is selected from the group consisting of a disease, a cancer, responses to an infection, responses to a therapeutic or toxic agent, and stages of development or aging.

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25. The method of claim 23, wherein the total number of said gene specific elements in (a) and (b) is from about 10 to about 1000.

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26. The method of claim 23, wherein the total number of said gene specific elements in (a) and (b) is from about 50 to about 300.

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27. The method of claim 23, wherein said genes commonly expressed in both control sample and in said tissue or said condition are common housekeeping genes or tissue specific genes.

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28. The method of claim 23, wherein said target sample comprises expressed RNAs or nucleic acid copies thereof, and wherein said gene specific elements spotted on said miniarray are selected from the group consisting of amplified cDNAs, cloned cDNAs, synthetic oligonucleotides and PNAs (proteins manufactured to mimic nucleic acid segments).

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29. The method of claim 23, wherein said target sample comprises expressed proteins, and wherein said gene specific elements spotted on said miniarray are selected subset of specific antibodies.

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30. The method of claim 23, wherein said visually distinct image comprises a pattern selected from the group consisting of a

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pattern that resembles a stoplight with clusters of red, yellow and green spots, alphanumeric characters, an abstract sign, a shape or symbol, and a simplified symbol or picture representing a tissue or condition.

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31. The method of claim 30, wherein said pattern is distinguished by a mean selected from the group consisting of difference in color, difference in intensity and location within said miniarray.

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32. The method of claim 30, wherein said shape or symbol is selected from the group consisting of triangles, rectangles, squares, circles, ovals, trapezoids, stars, hexagons, pentagons, octagons, bars, stripes, squiggles, rings, mathematical symbols and language symbols.

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33. The method of claim 30, wherein said simplified symbol or picture representing a tissue or condition is selected from the group consisting of a shape of a lung, a shape of a heart, a shape of a brain, a shape of a kidney, a shape of a stomach, a shape of a breast, a

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shape of a colon, a shape of a ragged rough-edged cell and a shape of a smooth round cells.

5   34.   The method of claim 23, wherein said gene specific elements corresponding to up-regulated genes and down-regulated genes are clustered in separated groups.

10   35.   The method of claim 34, wherein the clusters of gene specific elements corresponding to up-regulated and down-regulated genes are further subdivided into two or more subgroups based upon significant differences in modified expression levels in said tissue or said condition.

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           36.   The method of claim 23, wherein said gene specific elements are not clustered into specific groups on said miniarray, and said visually distinct image is generated by computer means.

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37. A method of diagnosis for specific tissue or condition using specialized diagnostic miniarrays targeted to the analysis of said tissue or condition, comprising the steps of:

(a) providing one or more target samples comprising gene expression products;

(b) constructing an addressable miniarray spotted with different binding elements;

(c) providing a set of intermediate probes comprising a specific binding element that binds to a specific gene expression product in a target sample and a generic binding element that binds to a matching binding element spotted on said addressable miniarray;

(d) binding said set of intermediate probes to said target sample(s) in solution hybridization conditions, wherein different target samples are handled separately and intermediate probes capable of binding with different reporter elements are bound to different target samples;

(e) capturing and washing the complex of gene expression products and bound intermediate probes to remove unbound intermediate probes;

(f) denaturing or removing said gene expression products if necessary to produce a subset of intermediate probes reflecting said

gene expression products and their relative frequency in the original sample;

(g) binding the resulting subset of intermediate probes to said addressable miniarray;

5   (f) examining the binding pattern of said subset of intermediate probes, wherein detection of a visually distinct image from said miniarray indicates the presence of said tissue or condition.

10   38.   The method of claim 37, wherein said reporter elements are selected from a group consisting of direct labeling agents, indirect label-binding molecules, haptens, and linker sequences that can bind a separate reporter selected from a group consisting of labeled DNA, GeneTAGs and ChipTAGs.

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39.   The method of claim 38, wherein said reporter elements or reporters are bound to the intermediate probes before or after said intermediate probes are bound to said miniarray.

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40. The method of claim 37, wherein said intermediate probes comprises:

(1) a first half-probe comprising a first binding element that binds to a first sequence in a target sample and a binding element that binds to a matching binding element spotted on said miniarray; and

(2) a second half-probe comprising a reporter element and a second binding element that binds to a second sequence in said target sample, wherein said first sequence and said second sequence are adjacent sequences in said target sample and said first half-probe and said second half-probe are joined together to form a singular unit by a ligase enzyme after binding to said first sequence and said second sequence.

41. The method of claim 37, wherein said intermediate probes are constructed as WRAP-Probes with universal linker/primer sequences at both ends, wherein increased signaling can be obtained by binding additional reporters to said universal linkers or exponentially amplifying said intermediate probes with a single primer set matching said primer sequences.

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42.   The method of claim 37, wherein said binding elements printed on said miniarray are generic oligonucleotides that are not substantially complementary to sequences of the target sample and that

5   constitute an arbitrary set of unique addresses and unique locations on said miniarray.

43.   The method of claim 37, wherein said binding elements

10   printed on said miniarray are organized in pre-defined patterns to facilitate the creation of said visually distinct image.

44.   The method of claim 37, wherein said miniarray is

15   printed with a small subset of binding elements that create different common capture areas on said miniarray to form said visually distinct image, wherein said intermediate probes are grouped into different groups that each has a common binding element which binds to a matching binding element spotted on said miniarray.

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45. The method of claim 44, wherein said groups of intermediate probes detect expression of genes selected from the group consisting of up-regulated genes in said tissue or condition, down-regulated genes in said tissue or condition, and genes with unchanged

5   expression levels in said tissue or condition as compared to control sample.

46. The method of claim 37, wherein said binding elements
10 printed on said miniarray are selected from the group consisting of avidin, streptavidin, anti-hapten antibody, anti-fluorescent dye antibody and anti-nonfluorescent dye antibody, wherein the matching binding elements on said intermediate probes are selected from the group consisting of biotin, hapten, fluorescent dye and nonfluorescent dye.

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47. The method of claim 46, wherein said hapten is selected from the group consisting of dinitrophenyl and nitrotyrosine.

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48. The method of claim 46, wherein said fluorescent dye or nonfluorescent dye is selected from the group consisting of digoxygenin, fluorescein, tetramethylrhodamine, Texas Red, dansyl, Alexa Fluor 488, BODIPY FL, lucifer yellow, Cascade Blue and Marina

5 Blue.

49. The method of claim 44, wherein said binding elements printed on said miniarray are generic oligonucleotides, wherein said intermediate probes are grouped into different groups that each has a

10 common binding element which binds to said oligonucleotides spotted on said miniarray.

50. The method of claim 37, wherein said condition is

15 selected from the group consisting of a disease, a cancer, responses to an infection, responses to a therapeutic or toxic agent, and stages of development or aging.

20 51. The method of claim 37, wherein said visually distinct image comprise pattern selected from the group consisting of a pattern

that resembles a stoplight with clusters of red, yellow and green spots, alphanumeric characters, an abstract sign, a shape or symbol, and a simplified symbol or picture representing a tissue or condition.

5   52. The method of claim 51, wherein said pattern is distinguished by a means selected from the group consisting of difference in color, difference in intensity and location within said miniarray.

10   53. The method of claim 51, wherein said shape or symbol is selected from the group consisting of triangles, rectangles, squares, circles, ovals, trapezoids, stars, hexagons, pentagons, octagons, bars, stripes, squiggles, rings, mathematical symbols and language symbols.

15   54. The method of claim 51, wherein said simplified symbol or picture representing a tissue or condition is selected from the group consisting of a shape of a lung, a shape of a heart, a shape of a brain, a shape of a kidney, a shape of a stomach, a shape of a breast, a shape of a colon, a shape of a ragged rough-edged cell and a shape of a

20   smooth round cells.